L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 202409-33-4 REGISTRY

CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 5-Chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-2,3'-bipyridine

CN Arcoxia

CN Etoricoxib

CN MK 0663

CN MK 663

FS 3D CONCORD

MF C18 H15 C1 N2 O2 S

CI COM

SR CA

LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

DT.CA CAplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

220 REFERENCES IN FILE CA (1907 TO DATE)

6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

223 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
L2
     26839-75-8 REGISTRY
RN
     2-Propanol, 1-[(1,1-dimethylethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-
CN
     thiadiazol-3-yl]oxy]-, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     1,2,5-Thiadiazole, 2-propanol deriv.
CN
     2-Propanol, 1-(tert-butylamino)-3-[(4-morpholino-1,2,5-thiadiazol-3-
     y1)oxy]-, (S)-(-)-(8CI)
     2-Propanol, 1-[(1,1-dimethylethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-
CN
     thiadiazol-3-yl]oxy]-, (S)-
OTHER NAMES:
     (-) -S-Timolol
CN
CN
     (-)-Timolol
CN
     (S)-Timolol
CN
     l-Timolol
CN
     L-Timolol
CN
     Oftensin
CN
     Timolol
FS
     STEREOSEARCH
     131628-37-0, 194288-09-0
DR
     C13 H24 N4 O3 S
MF
CI
     COM
LC
     STN Files:
                  ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST,
       CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT,
       IFIUDB, IMSCOSEARCH, IMSPATENTS, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR,
       PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL, VETU
         (*File contains numerically searchable property data)
                      EINECS**, NDSL**, TSCA**, WHO
     Other Sources:
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
       Roles from patents: ANST (Analytical study); BIOL (Biological study);
RL.P
       MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP
       (Properties); RACT (Reactant or reagent); USES (Uses)
       Roles for non-specific derivatives from patents: BIOL (Biological
RLD.P
       study); PREP (Preparation); USES (Uses)
      Roles from non-patents: ANST (Analytical study); BIOL (Biological
RL.NP
       study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
       (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
       reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical
       study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP
       (Preparation); PRP (Properties); RACT (Reactant or reagent)
```

Absolute stereochemistry. Rotation (-).

^{**}PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

- 1315 REFERENCES IN FILE CA (1907 TO DATE)
- 22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 1321 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

```
ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
L3
RN
     26921-17-5 REGISTRY
CN
     2-Propanol, 1-[(1,1-dimethylethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-
     thiadiazol-3-yl]oxy]-, (2S)-, (2Z)-2-butenedioate (1:1) (salt) (9CI) (CA
OTHER CA INDEX NAMES:
     1,2,5-Thiadiazole, 2-propanol deriv.
     2-Propanol, 1-(tert-butylamino)-3-[(4-morpholino-1,2,5-thiadiazol-3-
CN
     yl)oxy]-, (-)-, maleate (1:1) (salt) (8CI)
     2-Propanol, 1-[(1,1-dimethylethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-
     thiadiazol-3-yl]oxy]-, (S)-, (Z)-2-butenedioate (1:1) (salt)
OTHER NAMES:
     (-)-Timolol maleate
CN
CN
     (S)-(-)-Timolol maleate
CN
     (S)-Timolol hydrogen maleate
CN
     Aquanil
     Betim
CN
CN
     Betime
CN
     Blocadren
CN
     Blocanol
CN
     Istalol
CN
     L-Timolol maleate
CN
     1-Timolol maleate
CN
    MK 950
CN
     Optimol
CN
     Proflax
     Rysmon TG
CN
CN
     Temserin
CN
     Tenopt
CN
     Timabak
CN
     Timacar
CN
     Timacor
CN
     Timolol hydrogen maleate
CN
     Timolol LA
CN
     Timolol maleate
CN
     Timoptic
CN
     Timoptol
     Timoptol XE
CN
CN
     Timorom
CN
     WP 934
FS
     STEREOSEARCH
DR
     131628-38-1, 30166-36-0, 116475-10-6
MF
     C13 H24 N4 O3 S . C4 H4 O4
CI
     COM
LC
     STN Files:
                ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,
       BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS,
       CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB,
       IMSPATENTS, IPA, MRCK*, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*,
       TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:
                     EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P
       Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
       (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P
       Roles for non-specific derivatives from patents: BIOL (Biological
       study); USES (Uses)
       Roles from non-patents: ANST (Analytical study); BIOL (Biological
RL.NP
       study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP
       (Properties); RACT (Reactant or reagent); USES (Uses)
```

CM

CRN 26839-75-8

CMF C13 H24 N4 O3 S

Absolute stereochemistry. Rotation (-).

CM 2

CRN 110-16-7

=> d 111 1-10 bib, kwic

- L11 ANSWER 1 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- AN 1987:233574 BIOSIS
- DN PREV198783121744; BA83:121744
- TI TIMOLOL MALEATE A BETA BLOCKER IN THE TREATMENT OF COMMON MIGRAINE HEADACHE.
- AU GALLAGHER R M [Reprint author]; STAGLIANO R A; SPORAZZA C
- CS MED CENTER FOR HEADACHE, 513 SOUTH LENOLA ROAD, MOORESTOWN, NEW JERSEY 08057, USA
- SO Headache, (1987) Vol. 27, No. 2, pp. 84-86. CODEN: HEADAE. ISSN: 0017-8748.
- DT Article
- FS BA
- LA ENGLISH
- ED Entered STN: 22 May 1987 Last Updated on STN: 22 May 1987
- TI TIMOLOL MALEATE A BETA BLOCKER IN THE TREATMENT OF COMMON MIGRAINE HEADACHE.
- SO Headache, (1987) Vol. 27, No. 2, pp. 84-86. CODEN: HEADAE. ISSN: 0017-8748.
- Timolol maleate, a beta blocker, has been shown to reduce the frequency of common migraine headache in clinical trials. An analysis of 116 patients treated prophylactically for common migraine with timolol maleate 10-30 mg· per day was conducted. There were 35 males and 81 females ranging in age from 19.
 . . patients (20%) showed < 25% improvement, and 4 patients (3%) discontinued because of side effects. This limited study suggests that timolol maleate may be of benefit in the treatment of some migraine patients.
- RN 26921-17-5 (TIMOLOL MALEATE)
- L11 ANSWER 2 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- AN 1986:431759 BIOSIS
- DN PREV198631097571; BR31:97571
- TI TIMOLOL MALEATE A BETA BLOCKER IN THE TREATMENT OF COMMON MIGRAINE HEADACHE.
- AU GALLAGHER R M [Reprint author]; STAGLIANO R A
- CS MOORESTOWN, NJ, USA
- SO Headache, (1986) Vol. 26, No. 6, pp. 312.
 Meeting Info.: TWENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION
 FOR THE STUDY OF HEADACHE, CHICAGO, ILL., USA, JUNE 27-29, 1986. HEADACHE.
 CODEN: HEADAE. ISSN: 0017-8748.
- DT Conference; (Meeting)
- FS BR
- LA ENGLISH
- ED Entered STN: 25 Oct 1986 Last Updated on STN: 25 Oct 1986
- TI TIMOLOL MALEATE A BETA BLOCKER IN THE TREATMENT OF COMMON MIGRAINE HEADACHE.
- SO Headache, (1986) Vol. 26, No. 6, pp. 312.

 Meeting Info.: TWENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION
 FOR THE STUDY OF HEADACHE,. . .
- RN 26921-17-5 (TIMOLOL MALEATE)
- L11 ANSWER 3 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- AN 1982:232842 BIOSIS
- DN PREV198274005322; BA74:5322

Mud

- TI BLOCADREN TIMOLOL MALEATE IN THE TREATMENT OF MIGRAINE PILOT STUDY.
- AU LOVLAND B [Reprint author]
- CS LOKKEGARDEN LEGEKONTOR, 1400 SKI
- Tidsskrift for den Norske Laegeforening, (1981) Vol. 101, No. 29, pp. 1645-1646.

 CODEN: TNLAAH. ISSN: 0029-2001.
- DT Article
- FS BA
- LA NORWEGIAN
- TI BLOCADREN TIMOLOL MALEATE IN THE TREATMENT OF MIGRAINE PILOT STUDY.
- SO Tidsskrift for den Norske Laegeforening, (1981) Vol. 101, No. 29, pp. 1645-1646.

 CODEN: TNLAAH. ISSN: 0029-2001.
- AB Patients [23] with migraine were, after a wash-out period of 8 wk, treated with blocadren (timolol maleate) for 16 wk.

 Treatment efficacy was primarily evaluated as a reduction in the number of attacks per month and. . .
- RN 26921-17-5 (BLOCADREN) 26921-17-5 (TIMOLOL MALEATE)
- L11 ANSWER 4 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- AN 1980:253770 BIOSIS
- DN PREV198070046266; BA70:46266
- TI THERAPEUTIC USE OF BETA BLOCKERS IN GENERAL PATHOLOGY RHEUMATOLOGY NEUROLOGY AND OPHTHALMOLOGY.
- AU BOUVENOT G [Reprint author]; BARTOLIN R; ESCANDE M; DELBOY C
- CS SERV MED INTERN, HOTEL DIEU, 13224 MARSEILLE CEDEX 1, FR
- SO Therapie (London/Paris), (1980) Vol. 35, No. 1, pp. 61-82. CODEN: THERAP. ISSN: 0040-5957.
- DT Article
- FS BA
- LA FRENCH
- SO Therapie (London/Paris), (1980) Vol. 35, No. 1, pp. 61-82. CODEN: THERAP. ISSN: 0040-5957.
- AB. . . of Sudek's atrophy and spasmophilia with tachycardia. In neurology, $\beta\text{-blockers}$ are interesting in 60-80% of cases of all types of $\pmb{\text{migraine}};$ they decrease the amplitude of senile tremor but they are inactive on the parkinsonian tremor. In ophthalmology, the use of. .
- IT Miscellaneous Descriptors

 HUMAN CARDIO VASCULAR SYSTEM **TIMOLOL** MALEATE AUTONOMIC-DRUG

 OPHTHALMIC-DRUG SUDEKS ATROPHY SPASMOPHILIA TACHY CARDIA **MIGRAINE** SENILE TREMOR PARKINSONIAN TREMOR OPEN ANGLE GLAUCOMA
 PSYCHIATRY EYE DROP PHARMACODYNAMICS
- RN 26921-17-5 (TIMOLOL MALEATE)
- L11 ANSWER 5 OF 10 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
- AN 1998:28538277 BIOTECHNO
- TI Report to the Danish committee on adverse drug reactions INDBERETNING TIL BIVIRKNINGSNAEVNET
- CS Bivirkningsnaevn, Sundhedsstyrelsen, Frederikssundsvej 387, DK-2700 Bronshoj.
- SO Ugeskrift for Laeger, (23 NOV 1998), 160/48 (6996-6998), 20 reference(s)
 CODEN: UGLAAD ISSN: 0041-5782
- DT Journal; Note
- CY Denmark
- LA Danish
- SO Ugeskrift for Laeger, (23 Nov 1998), 160/48 (6996-6998), 20

reference(s)
CODEN: UGLAAD ISSN: 0041-5782

RN. . . 104632-26-0; (lepirudin) 138068-37-8; (sodium dihydrogen phosphate) 7558-80-7, 7632-05-5; (brimonidine) 59803-98-4; (lamivudine) 134678-17-4, 134680-32-3; (zidometacin) 62851-43-8; (mercaptamine) 156-57-0, 60-23-1; (navelbine) 71486-22-1; (timolol maleate) 26921-17-5; (dorzolamide) 130693-82-2; (ibandronic acid) 114084-78-5, 138844-81-2, 138926-19-9; (mizolastine) 108612-45-9; (prostavasin) 55648-20-9; (prostaglandin el) 745-65-3; (montelukast) 151767-02-1, 158966-92-8; (hyaluronic acid) 31799-91-4, . . .

L11 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:215996 CAPLUS

DN 138:8296

TI Facilitated delivery of timolol maleate by iontophoresis

AU Saraf, Swarnlata; Jain, S.; Dixit, V. K.

CS B.R. Nahata College of Pharmacy, 458 001, India

SO Indian Drugs (2001), 38(7), 376-379 CODEN: INDRBA; ISSN: 0019-462X

PB Indian Drug Manufacturers' Association

DT Journal

LA English

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Indian Drugs (2001), 38(7), 376-379 CODEN: INDRBA; ISSN: 0019-462X

AΒ Timolol maleate (TM) is a β -adrenergic blocker used in cardiovascular and respiratory complications like hypertension, glaucoma, angina pectoris, myocardial infarction and migraine. The iontophoretic technique has been used to enhance the delivery of TM through skin. It is a technique, which permeate ionic form of drugs across the membrane by passing the current through an electrolyte. Iontophoretic delivery of drugs is affected by physico-elec. factors like initial drug concentration, pH, ionic strength, and frequency. These factors were aimed to be optimized for the iontophoretic delivery of TM through the skin. The passive and iontophoretic drug skin permeation studies were conducted by 2-chambered horizontal diffusion cells and human cadaver skin. The iontophoretic permeation through skin was dependent on the ionic species of drug. By optimizing the pH and ionic strength of donor solution and frequency of current the iontophoretic permeability of TM can be enhanced.

IT 26921-17-5, Timolol maleate
 RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (delivery of timolol maleate by iontophoresis)

L11 ANSWER 7 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 96005820 EMBASE

DN 1996005820

```
Medications used to prevent migraine headaches and their
TI
     potential ocular adverse effects.
     Doughty M.J.; Lyle W.M.
ΑU
     Department of Vision Science, Glasgow-Caledonian University, Cowcaddens
CS
     Road, Glasgow G4 OBA, United Kingdom
     Optometry and Vision Science, (1995) 72/12 (879-891).
SO
     ISSN: 1040-5488 CODEN: OVSCET
CY
     United States
     Journal; Article
DT
             Neurology and Neurosurgery
FS
     008
             Ophthalmology
     012
             Drug Literature Index
     037
             Adverse Reactions Titles
     038
     English
LA
SL
     English
     Medications used to prevent migraine headaches and their
TI
     potential ocular adverse effects.
     Optometry and Vision Science, (1995) 72/12 (879-891).
SO
     ISSN: 1040-5488 CODEN: OVSCET
          . present a detailed review of the medications used in the USA,
AB
     Canada, and the United Kingdom for the prevention of migraine
     and the potential ocular adverse effects associated with the use of these
     medications. Those drugs that are administered for the purpose of reducing
     the frequency or severity of migraine attacks are classified
     according to whether they act on the cerebral vasculature primarily at
     serotonin (5-HT2) receptors (e.g., methysergide, cyproheptadine, and
     pizotyline), beta adrenergic (primarily beta-2) receptors (e.g.,
     propranolol and timolol), via central nervous system (CNS)
     adrenergic (alpha-2) receptors (e.g., clonidine), or calcium channels
     (e.g., flunarizine). The roles and mechanisms of action of tricyclic
     antidepressants (e.g., amitriptyline) and non-steroidal anti-inflammatory
     drugs (NSAIDs) in the prophylactic management of migraine are
     also discussed, along with possible pharmacogenetic differences in the
     kinetics of action of some of these drugs. The general.
     Medical Descriptors:
CT
     *eye disease: ET, etiology
     *eye disease: SI, side effect
       *migraine: PC, prevention
       *migraine: DT, drug therapy
     article
     conjunctivitis: SI, side effect
     diplopia: SI, side effect
     drug contraindication
     drug mechanism
     drug safety
     dry eye: SI, side effect
     food composition
     gastrointestinal symptom: SI, side.
     . . 21829-25-4; (phenethylamine) 64-04-0; (pizotifen) 15574-96-6;
RN.
     (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6;
      (reserpine) 50-55-5, 8001-95-4; (serotonin) 50-67-9; (timolol) 26839-75-8;
      (timolol maleate) 26921-17-5; (tryptamine) 343-94-2, 61-54-1;
      (tyramine) 51-67-2, 60-19-5
     ANSWER 8 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
L11
     on STN
AN
     85050077 EMBASE
     1985050077
DN
     [Antimigraine agents].
TI
     ANTIMIGRAINEUX.
     Rascol A.; Fanchamps A.
ΑU
```

```
Service de Neurologie, CHU Purpan, 31059 Toulouse Cedex, France
CS
     Semaine des Hopitaux, (1984) 60/44-45 (3137-3161).
SO
     CODEN: SHPAAI
CY
     France
DT
     Journal
FS
     038
             Adverse Reactions Titles
     037
             Drug Literature Index
     800
             Neurology and Neurosurgery
     030
             Pharmacology
     French
LA
     English
SL
     Semaine des Hopitaux, (1984) 60/44-45 (3137-3161).
SO
     CODEN: SHPAAI
     The definition of \ensuremath{\operatorname{migraine}} proposed by the ad hoc committee in
AΒ
     its classification of the different forms of headache is the most widely
     accepted. In this chapter, currently established physiopathological
     mechanisms of migraine attacks with the different stages of
     encephalic vasomotor disorders and the humoral changes which produce them
     are exposed. A description is given of the as yet incompletely understood
     constitutional anomalies that predispose to migraine; these
     include platelet function disorders currently considered as central, but
     also other factors such as hypersensitivity to dopamine or alterations.
        complied with. Ergot toxicity is usually the result of excessive dosage
     or overprolonged use. The chapter on maintenance therapy of
     migraine addresses only the most widely used drugs whose
     effectiveness has been established by controlled trials. Such drugs are
     numerous, have. . . stabilizers of vascular tone (dihydroergotamine,
     clonidine, flunarizine), substances that interfere with serotonin
     (methysergide, pizotifen, dimetotiazine, oxetorone), beta blocking agents
     (propranolol, timolol), platelet aggregation inhibitors
     (acetylsalicylic acid, dipyramidole), antidepressants (tricyclic
     antidepressants, lithium). Maintenance treatment is justified only if
     attacks recur frequently and.
     Medical Descriptors:
     *adverse drug reaction
     *artery spasm
     *drug interaction
       *migraine
     *pharmacokinetics
     *drug therapy
     peripheral vascular system
     muscle
     therapy
     human
     central nervous system
     *acebutolol
     *acetylsalicylic acid
     *alprenolol
     *aminophenazone
     *amitriptyline
     *antimigraine agent
     *atenolol
     *beta adrenergic receptor blocking agent
     *caffeine
     *clomipramine
     *clonidine
     *dexpropranolol
     *dihydroergotamine mesilate
     *dimetotiazine
     *ergotamine
     *ergotamine tartrate
     *flufenamic acid
```

```
*flunarizine
    *imipramine
    *lithium carbonate
     *mefenamic acid
     *methysergide
     *metoprolol
     *nadolol
     *oxetorone
     *oxprenolol
     *phenacetin
     *pindolol
     *pizotifen
     *practolol
     *propranolol
     *propyphenazone
     *timolol
    anticoagulant agent
     antihypertensive agent
     tuberculostatic agent
     cholinergic.
          363-24-6; (quinidine) 56-54-2; (sulfinpyrazone) 57-96-5;
RN.
     (troleandomycin) 2751-09-9; (tyramine) 51-67-2, 60-19-5; (verapamil)
     152-11-4, 52-53-9; (dipyridamole) 58-32-2; (oxetorone fumarate)
     34522-46-8; (timolol maleate) 26921-17-5; (pizotifen maleate)
     24359-22-6; (dimetotiazine mesylate) 13115-40-7
    ANSWER 9 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     85011557 EMBASE
     1985011557
    Migraine prevention with timolol. A double-blind
     crossover study.
     Stellar S.; Ahrens S.P.; Meibohm A.R.; Reines S.A.
     Department of Neurosurgery, St Barnabas Medical Center, Livingston, NJ
     07039, United States
     Journal of the American Medical Association, (1984) 252/18
     (2576-2580).
     CODEN: JAMAAP
     United States
     Journal
             Adverse Reactions Titles
     038
     037
             Drug Literature Index
     800
             Neurology and Neurosurgery
     030
             Pharmacology
     English
     Migraine prevention with timolol. A double-blind
     crossover study.
     Journal of the American Medical Association, (1984) 252/18
     (2576-2580).
     CODEN: JAMAAP
     One hundred seven patients (77 women and 30 men) with migraine
     headache were given prophylactic treatment with timolol maleate,
     20 to 30 mg/day, or matching placebo during a 20-week, double-blind
     crossover study. Among the 94 patients who completed the study,
     timolol was significantly better than placebo in terms of a
     decrease in frequency of headaches from baseline, numbers of patients who
     had a 50% reduction in headache frequency, global response, and patient
     preference. Overall global response rates were 65% with timolol
     compared with 40% with placebo. The severity and duration of headaches
     that occurred were unchanged. Few side effects were reported with either
     timolol or placebo. The study demonstrates that the \beta-blocker
     timolol is a safe and effective treatment in patients with
```

ΑN

DN

TI

ΑU

CS

SO

CY DT

FS

LA

ΤI

SO

ΑB

```
frequent migraine headaches.
CT
    Medical Descriptors:
    *adverse drug reaction
     *constipation
     *drug efficacy
     *fatique
     *gastrointestinal toxicity
     *insomnia
       *migraine
     *neurotoxicity
     *drug therapy
     *stomach pain
     *vertigo
    prevention
    priority journal
     large intestine
     stomach
     therapy
     intoxication
     nervous system
     oral drug administration
     human
     central nervous system
     controlled study
     major clinical study
     *timolol
     *timolol maleate
     acetylsalicylic acid
     butalbital
     caffeine
     ergotamine
     paracetamol
     placebo
     (timolol) .26839-75-8; (timolol maleate) 26921-17-5;
RN
     (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6,
     63781-77-1; (butalbital) 51005-25-5, 77-26-9; (caffeine) 30388-07-9,
     58-08-2; (ergotamine) 113-15-5, 52949-35-6; (paracetamol) 103-90-2
L11 ANSWER 10 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
AN
     83065958 EMBASE
     1983065958
DN
     The prophylactic effect of timolol versus propranolol and
TI
     placebo in common migraine: Beta-blockers in migraine.
ΑU
     Neurol. Dep., Ulleval Hosp., Oslo 1, Norway
CS
     Cephalalgia, (1982) 2/3 (165-170).
SO
     CODEN: CEPHDF
CY
     Norway
DТ
     Journal
             Neurology and Neurosurgery
FS
     800
             Drug Literature Index
     037
LΑ
     The prophylactic effect of timolol versus propranolol and
ΤI
     placebo in common migraine: Beta-blockers in migraine.
     Cephalalgia, (1982) 2/3 (165-170).
SO
     CODEN: CEPHDF
     A multicentre double-blind, cross-over trial was planned to evaluate the
AB
     prophylactic effect of timolol in migraine. The
     effectiveness of the drug was compared to propranolol and placebo. In the
     Norwegian part of the trial described in this paper, 18 patients completed
     the study. The data suggest that timolol is equivalent in
```

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effectiveness to propranolol in migraine prophylaxis. Firm
conclusions should not be drawn until the results from the multicentre
trial are available.
Medical Descriptors:
*headache
  *migraine
*drug therapy
therapy
human
central nervous system
prevention
clinical article
*placebo
*propranolol
*timolol
timolol maleate
(propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6;
```

(timolol) 26839-75-8; (timolol maleate) 26921-17-5

CT

RN

(FILE 'HOME' ENTERED AT 14:41:54 ON 15 DEC 2004)

FILE 'REGISTRY' ENTERED AT 14:42:04 ON 15 DEC 2004

- 1 S ETORICOXIB/CN
- L2 1 S TIMOLOL/CN
- L3 1 S (TIMOLOL MALEATE)/CN

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, ...' ENTERED AT 14:43:14 ON 15 DEC 2004

	OI TO DEC	3001
L4	3	S L1 AND L3
L5	62	S L1 AND MIGRAINE
L6	15	S L5 AND PD<2003
L7	14	DUP REM L6 (1 DUPLICATE REMOVED)
L8	94	S L3 AND MIGRAINE
L9	78	S L8 AND PD<2003
L10	74	DUP REM L9 (4 DUPLICATES REMOVED)
L11	10	S L10 AND (TIMOLOL (P) MIGRAINE)

=>

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2000:314539 CAPLUS
AN
     132:329940
DN
     Pharmaceutical compositions containing histaminergic agonist and COX-2
TI
     inhibitor for migraine treatment
     Simitchieva, Kremena; Reines, Scott A.; Mckinney, Errol; Sandquist, Eric
IN
     J.; Khanna, Deepak K.; Hargreaves, Richard
     Merck & Co., Inc., USA
PA
     PCT Int. Appl., 16 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
                                                                    DATE
     PATENT NO.
                         KIND
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                                            APPLICATION NO.
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                                                                    19991029
     WO 2000025779
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                         A1
PI
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             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
             MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
             SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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                                            JP 2000-579220
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     JP 2002528498
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                                            AU 2000-17098
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                                20030410
                                            US 2001-934823
                                                                    20010822
                                20020207
     US 2002016348
                          A1
     US 6384034
                                20020507 /
                          B2
     US 2002177617
                                            US 2002-106845
                                                                    20020326
                          A1
                                20021128
                                19981102
PRAI US 1998-106605P
                          Ρ
     US 1999-429274
                                19991029
                          Α1
     WO 1999-US25388
                          W
                                19991029
                                20010822
     US 2001-934823
                          A3
              THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 9
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
     Pharmaceutical compositions containing histaminergic agonist and COX-2
TI
     inhibitor for migraine treatment
     A combination of a 5HT1B/1D agonist and a cyclooxygenase-2 (COX-2)
AΒ
     selective inhibitor is useful in the treatment and/or prevention of
     migraine. The 5HT1B/1D agonist is selected from sumatriptan,
     naratriptan, zolmitriptan, eletriptan, almotriptan, and rizatriptan, and
     the COX-2 inhibitor is selected from meloxicam, MK-663
      Vioxx, RS 57067, celecoxib, and compound I. The 5HT1B/1D agonist and
     COX-2 inhibitor are administered combined in a single dosage form or as
     sep. dosage forms administered concurrently. Tablets containing 5 and 10 mg
     of rizatriptan benzoate and 10 mg Vioxx were prepared
     cyclooxygenase inhibitor histaminergic agonist tablet migraine
ST
IT
        (5-HT1B; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
IT
     5-HT agonists
        (5-HT1D; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
ΙT
     Antimigraine agents
         (tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
```

ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

L4

IT 39391-18-9, Cyclooxygenase

=>

RL: BSU (Biological study, unclassified); BIOL (Biological study) (2, inhibitors; tablets containing histaminergic agonist and COX-2 inhibitor for migraine treatment)

TT 71125-38-7, Meloxicam 103628-46-2, Sumatriptan 121679-13-8,
Naratriptan 139264-17-8, Zolmitriptan 143322-58-1, Eletriptan
144034-80-0, Rizatriptan 145202-66-0, Rizatriptan benzoate
154323-57-6, Almotriptan 162011-90-7, Vioxx 169590-42-5, Celecoxib
179382-91-3, RS 57067 180200-69-5 202409-33-4, MK
663

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tablets containing histaminergic agonist and COX-2 inhibitor for migraine treatment)

MG + CX2

```
ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
    2003:260861 CAPLUS
ΑN
    138:276275
DN
    Cyclooxygenase-2 inhibitor compositions with rapid onset of therapeutic
TΙ
     Kararli, Tugrul T.; Kontny, Mark J.; Desai, Subhash; Hageman, Michael J.;
IN
     Haskell, Royal J.; Hassan, Fred; Forbes, James C.
PA
    U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 731,350.
SO
     CODEN: USXXCO
DT
     Patent
LA
     English
FAN.CNT 11
     PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
                                                                 DATE
                        ____
                               _____
                                          ______
                                          US 2001-874504
    US 2003064098
                        A1
                               20030403
                                                                 20010605
PΤ
                               20021003
                                          US 2002-113157
                                                                 20020401 <---
    US 2002142045
                        A1
PRAI US 1999-169856P
                        P
                               19991209
     US 2000-731350
                        A2
                               20001206
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     US 2000-31898
                               20001206
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                               20001206
    WO 2000-US32434
                       A1
                               20010605
    US 2001-874504
    MARPAT 138:276275
OS
                       KIND
    PATENT NO.
                               DATE
                                         APPLICATION NO.
                                                                 DATE
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                                          ______
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                                          US 2001-874504
    US 2003064098
                        A1
                               20030403
                                                                 20010605
PΙ
    US 2002142045
                        A1
                               20021003 US 2002-113157
                                                                 20020401 <--
IT
    Headache
        (migraine; cyclooxygenase-2 inhibitor compns. with rapid
        onset of therapeutic effect)
     58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological
ΙT
     studies 69-89-6D, Xanthine, alkyl derivs. 83-67-0, Theobromine
     162011-90-7, Rofecoxib 169590-41-4, Deracoxib 181695-72-7, Valdecoxib
     202409-33-4 212126-32-4 215123-80-1
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (cyclooxygenase-2 inhibitor compns. with rapid onset of therapeutic
        effect)
     ANSWER 2 OF 14 USPATFULL on STN
L7
                                                      DUPLICATE 1
       2002:27500 USPATFULL
ΑN
       Method of treating migraines and pharmaceutical compositions
TI
IN
       Simitchieva, Kremena, Basking Ridge, NJ, UNITED STATES
       Reines, Scott A., New Hope, PA, UNITED STATES
       Mckinney, Errol, Doylestown, PA, UNITED STATES
       Sandquist, Eric J., Doylestown, PA, UNITED STATES
       Khannna, Deepak K., Furlong, PA, UNITED STATES
       Hargreaves, Richard, Terlings Park, UNITED KINGDOM
PA
      Merck & Co. Inc. (U.S. corporation)
                        A1
B2
РΤ
      US 2002016348
                              20020207
                                                                  <--
       US 6384034
                              20020507
       US 2001-934823
                        A1
                              20010822 (9)
AΤ
       Continuation of Ser. No. US 1999-429274, filed on 29 Oct 1999, PENDING
RLI
      US 1998-106605P 19981102 (60)
PRAI
      Utility
DΤ
FS
      APPLICATION
LREP
       RICHARD C. BILLUPS, Patent Department, Merck & Co. Inc., P.O. Box 2000,
       Rahway, NJ, 07065-0907
CLMN
       Number of Claims: 10
\mathsf{ECL}
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 331
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SUMM [0017] In one aspect of the invention, a method of treating or preventing migraine is disclosed in a mammalian patient in need of such treatment, which comprises administering to the patient a COX-2 selective. . .

SUMM [0026] An anti-migraine effective amount of the combination is that amount that will relieve the subject being treated of the symptoms of the migraine attack and the specific dose level and frequency of dosage may vary and will depend upon a variety of factors.

SUMM [0027] For the treatment of a migraine attack, the active ingredients, separately or in combination, may be administered orally, topically, parenterally, by inhalation, spray, rectally or intravaginally. . .

CLM What is claimed is:

1. A method of treating or preventing migraine in a mammalian patient in need of such treatment, which comprises administering to the patient a COX-2 selective inhibiting compound. . .

TT 71125-38-7, Meloxicam 103628-46-2, Sumatriptan 121679-13-8,
Naratriptan 139264-17-8, Zolmitriptan 143322-58-1, Eletriptan
144034-80-0, Rizatriptan 145202-66-0, Rizatriptan benzoate
154323-57-6, Almotriptan 162011-90-7, Vioxx 169590-42-5, Celecoxib
179382-91-3, RS 57067 180200-69-5 202409-33-4, MK 663
(tablets containing histaminergic agonist and COX-2 inhibitor for migraine treatment)

- L7 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 2002:964146 CAPLUS
- DN 138:39187
- TI Preparation of piperidinecarboxylates and related compounds as NMDA NR2B receptor antagonists for the treatment or prevention of ${\bf migraine}$
- IN Allen, Christopher; Koblan, Ken S.; Sleeth, Timothy
- PA Merck & Co., Inc., USA
- SO PCT Int. Appl., 185 pp.

CODEN: PIXXD2

- DT Patent
- LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2002-US21069
    WO 2002100352
                         A2
                                20021219
PΙ
                                20030327
    WO 2002100352
                         A3
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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     US 2004204341
                         A1
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                                20010612
PRAI US 2001-297672P
                                20020607
     WO 2002-US21069,
                         W
     Preparation of piperidinecarboxylates and related compounds as NMDA NR2B
TΙ
     receptor antagonists for the treatment or prevention of migraine
     WO 2002100352 A2 20021219
PΙ
                                          APPLICATION NO.
                                                                  DATE
                       KIND DATE
     PATENT NO.
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PΙ
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             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
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                         A2 20040324 EP 2002-744807
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                               20041014 US 2003-479923
                                                                   20031205
     US 2004204341
                         A1
     piperidinecarboxylate prepn NR2B receptor antagonist; migraine
ST
     treatment piperidinecarboxylate prepn
IT
     5-HT agonists
        (5-HT1B, coadministration; preparation of piperidinecarboxylates and related
        compds. as NR2B receptor antagonists for the treatment or prevention of
        migraine)
IT
     5-HT agonists
        (5-HT1D, coadministration; preparation of piperidinecarboxylates and related
        compds. as NR2B receptor antagonists for the treatment or prevention of
        migraine)
     Calcitonin gene-related peptide receptors
TT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ligands, coadministration; preparation of piperidinecarboxylates and
        related compds. as NR2B receptor antagonists for the treatment or
        prevention of migraine)
IT
     Headache
        (migraine, treatment; preparation of piperidinecarboxylates and
        related compds. as NR2B receptor antagonists for the treatment or
        prevention of migraine)
IT
     Antimigraine agents
        (preparation of piperidinecarboxylates and related compds. as NR2B receptor
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20020607 <--

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antagonists for the treatment or prevention of migraine)
     Glutamate receptors
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (preparation of piperidinecarboxylates and related compds. as NR2B receptor
        antagonists for the treatment or prevention of migraine)
                                121679-13-8, Naratriptan
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     103628-46-2, Sumatriptan
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     Zolmitriptan
                    143322-58-1, Eletriptan
                                158966-92-8, Montelukast
     154323-57-6, Almotriptan
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                                                                 181695-72-7,
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                 169590-42-5, Celecoxib
                                          180200-68-4, JTE522
                                          198470-84-7, Parecoxib
                  197438-48-5, BMS347070
     Valdecoxib
     202409-33-4, Etoricoxib
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                                                       221148-46-5
                            346670-87-9, CS 502 (pharmaceutical)
     266320-83-6, ABT 963
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (coadministration; preparation of piperidinecarboxylates and related compds.
        as NR2B receptor antagonists for the treatment or prevention of
        migraine)
     455265-37-9P
IT
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (preparation of piperidinecarboxylates and related compds. as NR2B receptor
        antagonists for the treatment or prevention of migraine)
ΙT
     366022-97-1P
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                             455265-20-0P, Benzyl 4-[[(3-
     piperidinecarboxylate
                                                        455265-21-1P, Benzyl
     pyridinyl)amino]methyl]-1-piperidinecarboxylate
     4-[(3-isoxazolylamino)methyl]-1-piperidinecarboxylate
                                                              455265-23-3P
                    455265-25-5P, 4-[(3-Methylpyridin-4-
     455265-24-4P
     ylamino)methyl]piperidine-1-carboxylic acid benzyl ester
                                                                 455265-27-7P,
     Benzyl 4-[[(4-methyl-2-pyridinyl)amino]methyl]-1-piperidinecarboxylate
     455265-28-8P, Benzyl 4-[(1,3,4-thiadiazol-2-ylamino)methyl]-1-
     piperidinecarboxylate
                            455265-30-2P
                                            455265-31-3P
                                                            455265-32-4P, Benzyl
     4-[[(2-pyridinyl)amino]methyl]-1-piperidinecarboxylate
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     Benzyl 4-[[(4-ethyl-2-pyridinyl)amino]methyl]-1-piperidinecarboxylate
     455265-34-6P, Benzyl 4-[[(1-oxido-4-pyridinyl)amino]methyl]-1-
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     piperidinecarboxylate
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                                               478552-68-0P, Benzyl
 4-[[(1-methyl-1H-imidazol-2-yl)amino]methyl]-1-piperidinecarboxylate
 478552-69-1P, 4-(Quinolin-2-ylaminomethyl)piperidine-1-carboxylic acid
 benzyl ester
                478552-71-5P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
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                           55-22-1, Isonicotinic acid, reactions
                                                                     87 - 42 - 3,
 51-21-8, 5-Fluorouracil
                  96-50-4, 2-Aminothiazole
 6-Chloropurine
                                              99-96-7, 4-Hydroxybenzoic
 acid, reactions
                   100-46-9, Benzylamine, reactions
                                                       100-52-7
 Benzaldehyde, reactions
                          100-54-9, 3-Cyanopyridine
 Benzenepropanal 108-00-9, N,N-Dimethylethylenediamine
                                                             122 - 59 - 8,
 Phenoxyacetic acid
                     123-38-6, Propionaldehyde, reactions
                          155-10-2, 2-Chloro-5-fluoropyrimidin-4-ylamine
 3,6-Dichloropyridazine
                             456-47-3, 3-Fluorobenzyl alcohol
 372-48-5, 2-Fluoropyridine
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                   499-80-9, 2,4-Pyridinedicarboxylic acid
 3-Aminopyridine
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 3-Phenylpropionic acid
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 2-Aminopyridine
                   578-68-7, 4-Aminoquinoline
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                  626-60-8, 3-Chloropyridine
                                                626-61-9, 4-Chloropyridine
 isothiocyanate
 645-45-4, Hydrocinnamoyl chloride 676-58-4, Methylmagnesium chloride
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471248-78-9P

471248-83-6P

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695-34-1, 2-Amino-4-methylpyridine
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1450-93-7, 2-Aminoimidazole hemisulfate
                                       1603-40-3, 2-Amino-3-
methylpyridine
                1603-41-4, 2-Amino-5-methylpyridine
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1722-12-9, 2-Chloropyrimidine
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2,4-Dichloro-5-methylpyrimidine 1875-88-3, 2-(4-Chlorophenyl)ethanol
1990-90-5, 4-Amino-3-methylpyridine
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2-(2-Fluorophenyl)ethanol
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3-(2-Aminomethyl)pyridine
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2,4-Dichloropyrimidine 4005-51-0, 2-Amino-1,3,4-thiadiazole
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2,3-Dichloropyrazine
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2,4-Dichloro-6-methylpyrimidine 5440-17-5
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1-Benzyl-4-hydroxypiperidine-4-carbonitrile
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4-Methylthiopteridine
7144-05-0, 4-Aminomethylpiperidine 7461-50-9, 2-Chloropyrimidin-4-
         7589-27-7, 2-(4-Fluorophenyl)ethanol
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1-[(Benzyloxy)carbonyl]-4-piperidinecarboxylic acid
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Potassium thioacetate 13036-57-2, 2-Chloro-4-methylpyrimidine
            13534-90-2, 3,4-Dibromopyridine 17012-21-4
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4-Bromopyridine hydrochloride 20781-20-8, 2,4-Dimethoxybenzylamine
20928-46-5 22282-75-3, 3-Fluoro-4-iodopyridine
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2-Chloro-5-methylpyrimidine
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acid amide
Cyclopropylmagnesium bromide 24225-89-6, 1,4-Dibenzyl-2-
chloromethylpiperazine 27048-04-0, 6-Chloro-3-nitropyridin-2-ylamine
33252-32-3, 2-Amino-4-ethylpyridine
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Phenylcyclopropanecarboxaldehyde
                                 39514-19-7, Ethyl N-benzyl-3-
oxopiperidine-4-carboxylate 49844-90-8, 4-Chloro-2-methylthiopyrimidine
51171-02-9, 3-Bromopyrazine-2-carboxylic acid methyl ester
Ethyl 4-iodobenzoate 52147-97-4 52334-53-9, 4-Aminopyridin-3-ol
52763-21-0, Ethyl N-benzyl-3-oxopiperidine-4-carboxylate hydrochloride
59870-43-8, 2-Chloroquinazolin-4-ylamine
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N-[(4-Chlorobenzyloxy)carbonyloxy]succinimide
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Thiophen-3-ylmethanol 79521-61-2
4-pyridinamine 110859-47-7 128595-01-7 138163-08-3, Benzyl
4-formyl-1-piperidinecarboxylate 148148-48-5
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2-tert-Butoxycarbonylaminopyrimidine-5-carboxylic acid
N-[(4-Fluorobenzyloxy)carbonyloxy]succinimide 455267-67-1,
4-Methylbenzyl 4-(aminomethyl)-1-piperidinecarboxylate
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455267-76-2
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              455267-80-8
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carboxylate
1H-Pyrazole-4-carboxylic acid (piperidin-4-ylmethyl) amide
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4-Hydroxy-N-piperidin-4-ylmethylbenzamide 471254-22-5
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2,4-Dichloro-5-fluoropyrimidine 14161-11-6P, 3,4,5-Trichloropyridazine
21908-08-7P, 2-Formylisonicotinic acid ethyl ester 23504-39-4P,
2-(Diethyloxymethyl)isonicotinic acid ethyl ester 23804-68-4P,
4-Aminomethyl-1-benzylpiperidin-4-ol 35391-85-6P, 4-Cyclopropylbenzoic
acid ethyl ester 39478-61-0P, 1-Benzyl-4-hydroxymethylpiperidin-3-ol
41438-38-4P, 2,4-Pyridinedicarboxylic acid diethyl ester
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2-Chloro-5-fluoropyrimidine 85151-16-2P
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4-[(4-pyridinylamino)carbonyl]-1-piperidinecarboxylate
115687-29-1P, 1-Benzylpyrrolidine-3-carboxylic acid amide
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carboxylic acid tert-butyl ester 155456-33-0P 157023-34-2P, Benzyl

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4-(aminomethyl)piperidine-1-carboxylate
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     (cis)-3-Hydroxy-4-hydroxymethylpiperidine-1-carboxylic acid benzyl ester
    315717-77-2P, 3-Aminomethylpyrrolidine-1-carboxylic acid benzyl ester
                    454678-87-6P, (4-Cyclopropylphenyl) methanol
    405219-34-3P
    455267-05-7P, Benzyl 4-[[(1-oxido-4-pyridinyl)amino]carbonyl]-1-
                                            455267-07-9P, (cis)-3-Hydroxy-4-
    piperidinecarboxylate
                             455267-06-8P
     [(2,3,5,6-tetrachloropyridin-4-ylamino)methyl]piperidine-1-carboxylic acid
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     471254-16-7P, N-(1,4-Dibenzylpiperazin-2-ylmethyl)-4-hydroxybenzamide
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     471254-17-8P, 4-Hydroxy-N-piperazin-2-ylmethylbenzamide
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    N-(4-Benzylmorpholin-2-ylmethyl)-4-hydroxybenzamide
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     acid benzyl ester
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     329900-75-6, Cyclooxygenase-2
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     2002:868732 CAPLUS
     137:363084
     Use of cyclooxygenase inhibitors for treating migraines
    Allen, Christopher; Stone, Phyllis; Harper, Sean
    Merck & Co., Inc., USA
     PCT Int. Appl., 15 pp.
     CODEN: PIXXD2
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     50-33-9, Phenylbutazone, biological studies
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     22204-53-1, Naproxen 22494-42-4, Diflunisal
     Dihydroergocornine
                         25447-66-9, Dihydroergocryptine
                                                             25614-03-3,
                     26171-23-3, Tolmetin 29679-58-1, Fenoprofen
     Bromocriptine
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     34042-85-8, Sudoxicam 36322-90-4, Piroxicam 38194-50-2, Sulindac
     41340-25-4, Etodolac 42924-53-8, Nabumetone 51803-78-2, Nimesulide
     59804-37-4, Tenoxicam 70374-39-9, Lornoxicam 71125-38-7, Meloxicam
     74103-06-3, Ketorolac
                            76866-93-8 87234-24-0, Cinnoxicam
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     Rofecoxib 202409-33-4
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (use of cyclooxygenase inhibitors for treating migraines)
L7
     ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ΑN
     2002:813958 CAPLUS
DN
     137:316089
ΤI
     Oral pharmaceutical compositions comprising a low-water-soluble drug, a
     solvent, a fatty acid and an organic amine
     Ṣao, Ping; Karim, Aziz; Hassan, Fred; Forbes, James C.
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SO
     PCT Int. Appl., 67 pp.
     CODEN: PIXXD2
DT
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LΑ
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IT
     Headache
        (migraine; oral pharmaceutical compns. comprising
        low-water-soluble drug and solvent and fatty acid and organic amine)
IT
     57-10-3, Palmitic acid, biological studies 57-11-4, Stearic acid,
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     69-89-6D, Xanthine, alkyl derivs. 77-86-1, Tromethamine
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     111-42-2, Diethanolamine, biological studies 112-79-8, Elaidic acid
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112-80-1, Oleic acid, biological studies 124-07-2, Octanoic acid,

PΑ

Pharmacia Corporation, USA

141-43-5, Monoethanolamine, biological studies biological studies 142-62-1, Caproic acid, biological studies 143-07-7, Lauric acid, biological studies 334-48-5, Capric acid 463-40-1, Linolenic acid 506-30-9, Eicosanoic acid 544-63-8, Myristic acid, biological studies 13296-76-9, Eleostearic acid 25322-68-3, Polyethylene glycol 32839-30-8, Eicosapentaenoic acid 162011-90-7, Rofecoxib 32839-18-2 169590-41-4, Deracoxib 181695-72-7, Valdecoxib 202409-33-4, 212126-32-4 215123-80-1 Etoricoxib 266320-83-6 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oral pharmaceutical compns. comprising low-water-soluble drug and solvent and fatty acid and organic amine) ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN 2002:555346 CAPLUS 137:114529 Pharmaceutical composition having reduced tendency for drug crystallization Gao, Ping; Hageman, Michael J.; Morozowich, Walter; Dalga, Robert J.; Stefanski, Kevin J.; Huang, Tiehua; Karim, Aziz; Hassan, Fred; Forbes, James C. Pharmacia Corporation, USA PCT Int. Appl., 65 pp. CODEN: PIXXD2 Patent English FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE _____ ____ _____ ______ -----WO 2002056878 A2 20020725 WO 2002-US971 20020115 <--WO 2002056878 A3 20021219 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG 20021024 US 2002-47902 US 2002156124 Α1 20020114 <--CA 2434338 AA20020725 CA 2002-2434338 20020115 <--US 2003045563 A1 20030306 US 2002-47222 20020115 EP'1365812 A2 20031203 EP 2002-709027 20020115 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR BR 2002006580 A 20031216 BR 2002-6580 20020115 JP 2004520359 Т2 20040708 JP 2002-557386 -20020115 NO 2003003244 Α 20030917 NO 2003-3244 20030717 PRAI US 2001-262555P Ρ 20010118 P US 2001-284608P 20010417 WO 2002-US971 W 20020115 MARPAT 137:114529 WO 2002056878 A2 20020725 PATENT NO. DATE APPLICATION NO. KIND DATE _____ -----____ _____ WO 2002056878 A2 20020725 WO 2002-US971 20020115 <--WO 2002056878 A3 20021219 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

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             TJ, TM
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IT
     Headache
        (migraine; pharmaceutical composition having reduced tendency for
        drug crystallization)
IT
     56-81-5, Glycerin, biological studies
                                             58-08-2, Caffeine, biological
               58-55-9, Theophylline, biological studies
                                                            69-89-6D, Xanthine,
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                     83-67-0, Theobromine 9003-39-8, PVP
                                                             9004-32-4,
                                           9004-34-6D, Cellulose, derivs.
     Carboxymethyl cellulose sodium salt
     9004-54-0, Dextran, biological studies
                                              9004-57-3, Ethyl cellulose
     9004-64-2, Hydroxypropyl cellulose 9004-65-3, HPMC
                                                            9004-67-5, Methyl
                 25322-68-3, Polyethylene glycol 162011-90-7, Rofecoxib
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                             181695-72-7, Valdecoxib 202409-33-4,
     169590-41-4, Deracoxib
     Etoricoxib
                  212126-32-4
                                215123-80-1
                                              266320-83-6
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical composition having reduced tendency for drug
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     ANSWER 7 OF 14 USPATFULL on STN
L7
AN
       2002:315130 USPATFULL
TI
       Method of treating migraines and pharmaceutical compositions
       Simitchieva, Kremena, Basking Ridge, NJ, UNITED STATES
İΝ
       Reines, Scott A., New Hope, PA, UNITED STATES
       McKinney, Errol, Doylestown, PA, UNITED STATES
       Sandquist, Eric J., Doylestown, PA, UNITED STATES
       Khannna, Deepak K., Furlong, PA, UNITED STATES
       Hargreaves, Richard, Terlings Park, UNITED KINGDOM
PA
       Merck & Co., Inc. (U.S. corporation)
PΙ
       US 2002177617
                          A1
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       US 2002-106845
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ΑI
RLT
       Division of Ser. No. US 2001-934823, filed on 22 Aug 2001, GRANTED, Pat.
       No. US 6384034 Continuation of Ser. No. US 1999-429274, filed on 29 Oct
       1999, ABANDONED
       US 1998-106605P
PRAI
                           19981102 (60)
DT
       Utility
       APPLICATION
FS
       MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
LREP
CLMN
       Number of Claims: 10
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       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 330
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PΙ
       US 2002177617
                          A1
                               20021128
       A combination of a 5HT.sub.1B/1D agonist and a COX-2 selective inhibitor
AB
       is useful in the treatment and or prevention of migraine.
SUMM
       . . . has been known for some time that sumatriptan, which causes
       constriction of cranial blood vessels, is an effective treatment for
       migraine (see, for example, Doenicke et al., Lancet, 1988, Vol.
       1, 1309-11; and Feniuk & Humphrey, Drug Development Research, 1992, 26,.
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. . . within the trigeminal nucleus caudalis. It is believed that one
SUMM
       or more of these three mechanisms is involved in the anti-
       migraine action of 5-HT.sub.1B/1D receptor agonists such as
       rizatriptan.
       . . . method of treating or preventing migraines in a mammalian
SUMM
       patient in need thereof, which comprises administering to said patient
       an anti-migraine effective amount of a combination of a COX-2
       selective inhibitor and a 5-HT.sub.1B/1D receptor agonist.
SUMM
       [0010] One embodiment of the present invention is a method of treating
       or preventing migraine with an anti-migraine
       effective amount of a combination of a 5HT.sub.1B/1D agonist and a COX-2
       selective inhibitor. Another embodiment of the invention is.
       [0015] In one aspect of the invention, a method of treating or
SUMM
       preventing migraine is disclosed in a mammalian patient in
       need of such treatment, which comprises administering to the patient a
       COX-2 selective.
       [0024] An anti-migraine effective amount of the combination is
SUMM
       that amount that will relieve the subject being treated of the symptoms
       of the migraine attack and the specific dose level and
       frequency of dosage may vary and will depend upon a variety of factors.
SUMM
       [0025] For the treatment of a migraine attack, the active
       ingredients, separately or in combination, may be administered orally,
       topically, parenterally, by inhalation, spray, rectally or
       intravaginally.
CLM
       What is claimed is:
       1. A method of treating or preventing migraine in a mammalian
       patient in need of such treatment, which comprises administering to the
       patient a COX-2 selective inhibiting compound.
      71125-38-7, Meloxicam 103628-46-2, Sumatriptan
IT
                                                         121679-13-8,
      Naratriptan
                   139264-17-8, Zolmitriptan 143322-58-1, Eletriptan
      144034-80-0, Rizatriptan
                                 145202-66-0, Rizatriptan benzoate
      154323-57-6, Almotriptan
                               162011-90-7, Vioxx 169590-42-5, Celecoxib
      179382-91-3, RS 57067
                            180200-69-5 202409-33-4, MK 663
        (tablets containing histaminergic agonist and COX-2 inhibitor for migraine
        treatment)
     ANSWER 8 OF 14 USPATFULL on STN
L7
       2002:221058 USPATFULL
AN
ΤI
       Oral fast-melt formulation of a cyclooxygenase-2 inhibitor
IN
       Le, Trang T., Mundelein, IL, UNITED STATES
       Kararli, Tugrul T., Skokie, IL, UNITED STATES
       Kontny, Mark J., Libertyville, IL, UNITED STATES
       Sastry, Srikonda V., Sunnyvale, CA, UNITED STATES
       Nyshadham, Janaki R., Fremont, CA, UNITED STATES
       Pagliero, Arthur J., JR., Vacaville, CA, UNITED STATES
PI
       US 2002119193
                               20020829
                         A1
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ΑI
       US 2001-932494
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                               20010817 (9)
       US 2000-226349P
                          20000818 (60)
PRAI
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       APPLICATION
LREP
       Pharmacia Corporation, Corporate Patent Dept., 800 N. Lindbergh
       Boulevard - 04B, St. Louis, MO, 63167
CLMN
       Number of Claims: 89
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       Exemplary Claim: 1
DRWN
       No Drawings
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       US 2002119193
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                          Α1
                               20020829
SUMM
       [0061] Such compositions are useful in treating inflammation in such
       diseases as migraine headaches, periarteritis nodosa,
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thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic
       fever, type I diabetes, neuromuscular junction disease including
       myasthenia gravis,.
       [0074] For pain management generally and specifically for treatment and
SUMM
       prevention of headache and migraine, such compositions of the
       invention can be used to provide a daily dosage of celecoxib of about 50
       mg to. .
SUMM
       [0083] In an embodiment of the invention, particularly where the
       cyclooxygenase-2 mediated condition is headache or migraine,
       the present selective cyclooxygenase-2 inhibitory drug composition is
       administered in combination therapy with a vasomodulator, preferably a
       xanthine derivative having.
SUMM
       . . . vasomodulator or alkylxanthine are selected to be
       therapeutically and/or prophylactically effective for relief of pain
       associated with the headache or migraine. Suitable dosage
       amounts will depend on the particular selective cyclooxygenase-2
       inhibitory drug and the particular vasomodulator or alkylxanthine
       selected. For.
IT
      162011-90-7, Rofecoxib
                               169590-41-4, Deracoxib
                                                        169590-42-5, Celecoxib
      181695-72-7, Valdecoxib 202409-33-4, Etoricoxib
                                                        212126-32-4
      215123-80-1
                    266320-83-6
        (oral fast-melt formulation of cyclooxygenase-2 inhibitor)
     ANSWER 9 OF 14 USPATFULL on STN
L7
       2002:199141 USPATFULL
AN
       Rapid-onset formulation of a selective cyclooxygenase-2 inhibitor
ΤI
IN
       Hariharan, Madhusudan, Evanston, IL, UNITED STATES
       Kararli, Tugrul T., Skokie, IL, UNITED STATES
       Hassan, Fred, Peapack, NJ, UNITED STATES
       Forbes, James C., Glenview, IL, UNITED STATES
       US 2002107250
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PΙ
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       US 2001-836905
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                               20010417 (9)
AΤ
PRAI
       US 2000-197746P
                           20000418 (60)
       Utility
DT
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FS
       Pharmacia Corporation, P.O. Box 5110, Chicago, IL, 60680-5110
LREP
       Number of Claims: 38
CLMN
       Exemplary Claim: 1
ECL
       2 Drawing Page(s)
DRWN
LN.CNT 1552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PΙ
       US 2002107250
                         A1
                               20020808
AB
         . . and is useful in treatment of cyclooxygenase-2 mediated
       conditions and disorders, particularly pain. For relief of pain in
       headache or migraine, the composition can optionally be
       administered together with a vasodilator.
SUMM
         . . disclose compositions comprising a selective COX-2 inhibitory
       drug, a 5HT.sub.1 receptor agonist and caffeine, said to be useful for
       treating migraine.
       . . . immediate therapeutic effect than standard dosage forms. For
SUMM
       example, in the treatment of acute pain, for example in headache or
       migraine, rapid-onset dosage forms would be useful to provide
       fast pain relief.
SUMM
          . . important advance in the art to provide an effective method of
       treatment of acute pain, for example in headache or migraine,
       using such a formulation.
       . . selective COX-2 inhibitory drug composition of the invention.
SUMM
       In another embodiment, a method of treatment and/or prevention of
       headache or migraine is provided comprising orally
       administering, to a subject in need of such treatment or prevention, an
       aminosulfonyl-comprising selective COX-2 inhibitory.
       [0212] Such compositions are useful in treating inflammation in such
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diseases as migraine headaches, periarteritis nodosa, thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic fever, type I diabetes, neuromuscular junction disease including myasthenia gravis,. . .

- DETD . . . for treatment of acute COX-2 mediated disorders, especially for relief of pain, for example in headache, including sinus headache and migraine.
- DETD . . . surgery pain, post-general surgery pain, post-orthopedic surgery pain, and acute flares of osteoarthritis), for prevention and treatment of headache and migraine, for treatment of Alzheimer's disease, and for colon cancer chemoprevention.
- DETD [0226] For pain management generally and specifically for treatment and prevention of headache and migraine, compositions of the invention can be used to provide a daily dose of celecoxib of about 50 mg to about. . .
- DETD [0234] In an embodiment of the invention, particularly where the COX-2 mediated condition is headache or migraine, the present selective COX-2 inhibitory drug composition is administered in combination therapy with a vasomodulator, preferably a xanthine derivative having. . .
- DETD . . . vasomodulator or alkylxanthine are selected to be therapeutically and/or prophylactically effective for relief of pain associated with the headache or migraine. Suitable dosage amounts will depend on the particular selective COX-2 inhibitory drug and the particular vasomodulator or alkylxanthine selected. For. . CLM What is claimed is:
 - . cyclooxygenase-2 inhibitory drug and the vasomodulator are present in total and relative amounts effective to relieve pain in headache or migraine.
 - . inhibitory drug and the alkylxanthine compound are present in total and relative amounts effective to relieve pain in headache or migraine.
 - 33. The method of claim 32 wherein the subject suffers from headache or migraine and wherein there is further orally administered to the subject a vasomodulator, the selective cyclooxygenase-2 inhibitory drug and the vasomodulator being administered in total and relative amounts effective to relieve pain in the headache or migraine.
 - 35. The method of claim 32 wherein the subject suffers from headache or migraine and wherein there is further orally administered to the subject an alkylxanthine compound, the selective cyclooxygenase-2 inhibitory drug and the alkylxanthine compound being administered in total and relative amounts effective to relieve pain in the headache or migraine.
- ΙT 58-08-2, Caffein, biological studies 58-55-9, Theophylline, biological 69-89-6D, Xanthine, alkyl derivs. 83-67-0, Theobromine 110-71-4, Ethylene glycol dimethyl ether 110-80-5, Ethylene glycol monoethyl ether 111-76-2, Ethylene glycol monobutyl ether Diethylene glycol monomethyl ether 111-90-0, Diethylene glycol monoethyl ether 111-96-6, Diethylene glycol dimethyl ether Diethylene glycol diethyl ether 112-48-1, Ethylene glycol dibutyl ether 112-49-2, Triethylene glycol dimethyl ether 112-50-5, Triethylene glycol monoethyl ether 112-73-2, Diethylene glycol dibutyl ether 122-99-6, Ethylene glycol monophenyl ether 124-07-2D, Caprylic acid, 143-22-6, Triethylene glycol monobutyl ether glycerides 143-24-8, Tetraethylene glycol dimethyl ether 334-48-5D, Capric acid, glycerides 622-08-2, Ethylene glycol monobenzyl ether 629-14-1, Ethylene glycol diethyl ether 764-99-8, Diethylene glycol divinyl ether 18912-80-6, Diethylene glycol monoisobutyl ether 37321-62-3, Propylene glycol

68958-64-5, Polyoxyethylene glyceryl trioleate 63980-40-5 162011-90-7, Rofecoxib 169590-41-4, Deracoxib 156259-68-6, Capmul mcm 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 202409-33-4, 215123-80-1 247074-38-0 266320-83-6 212126-32-4 (rapid-onset formulation of selective cyclooxygenase-2 inhibitors) ANSWER 10 OF 14 USPATFULL on STN 2002:149172 USPATFULL Selective cyclooxygenase-2 inhibitors and vasomodulator compounds for generalized pain and headache pain Hassan, Fred, Peapack, NJ, UNITED STATES Forbes, James C., Skokie, IL, UNITED STATES US 2002077328 A1 20020620 <--US 2001-905292 **A**1 20010713 (9) 20010606 (60) US 2001-296196P US 2001-284248P 20010417 (60) US 2000-218101P 20000713 (60) Utility APPLICATION SENNIGER POWERS LEAVITT AND ROEDEL, ONE METROPOLITAN SQUARE, 16TH FLOOR, ST LOUIS, MO, 63102 Number of Claims: 125 Exemplary Claim: 1 10 Drawing Page(s) LN.CNT 4527 CAS INDEXING IS AVAILABLE FOR THIS PATENT. US 2002077328 A1 20020620 . . disclose compositions comprising a selective COX-2 inhibitory drug, a 5HT.sub.1 receptor agonist and caffeine, said to be useful for treating migraine. . . immediate therapeutic effect than standard dosage forms. For example, in the treatment of acute pain, for example in headache or migraine, rapid-onset dosage forms would be useful to provide fast pain relief. . . . mechanisms giving rise to pain, especially headache pain. Under the vasogenic theory, intracranial vasoconstriction was responsible for the symptoms of migraine aura and headache resulted from a rebound dilation and distention of cranial vessels and activation of perivascular nociceptive axons. However, under the alternate nerogenic theory, the brain generates the migraine and susceptibility to migraine attacks reflects thresholds intrinsic to the individual's brain. Thus, vascular changes occurring during migraine are the result and not the cause of the attack. Even considering the alternate theories of migraine, vascular changes are implicated as an important event during the headache. Thus, using a vasomodulator to affect vascular changes in. . . . cyclooxygenase-2 inhibitor compound a vasomodulator, the pain can be generalized pain or headache pain. The headache pain can be from migraine headache pain, cluster headache pain, chronic daily headache pain, substance-induced headache pain, tension or stress related headache pain, sinus headache. . . arteritis, or headache pain resulting from lumbar puncture. A very important preference for this invention is pain which results from migraine pain. Another important preference in the present invention is pain resulting from a cluster headache. Another preferred source of pain. What is claimed is: 11. The combination according claim 10 wherein the headache pain is selected from the group consisting of migraine headache pain,

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PRAI

111. The method according to claim 106 wherein the pain is selected from

cluster headache pain, chronic headache pain, substance-induced headache pain, tension or stress related headache pain, sinus headache pain,.

the group consisting of migraine headache pain, cluster headache pain, chronic headache pain, substance-induced headache pain, tension or stress related headache pain, sinus headache pain,. 162011-90-7, Rofecoxib IT254-04-6D, Benzopyran, derivs. 169590-41-4, 169590-42-5, Celecoxib 181695-72-7, Valdecoxib Deracoxib 198470-84-7, Parecoxib **202409-33-4**, Etoricoxib 212126-32-4 266320-83-6 (cyclooxygenase 2 inhibitors for treatment and prevention of ocular COX-2-mediated disorders) L7 ANSWER 11 OF 14 USPATFULL on STN ΑN 2002:140876 USPATFULL TΙ Rapidly disintegrating oral formulation of a cyclooxygenase-2 inhibitor IN Kararli, Tugrul T., Skokie, IL, UNITED STATES Kontny, Mark J., Libertyville, IL, UNITED STATES Le, Trang T., Mundelein, IL, UNITED STATES PΙ US 2002071857 A1 20020613 <--20010817 (9) ΑI US 2001-932537 A1 PRAI US 2000-226487P 20000818 (60) DTUtility FS APPLICATION LREP Pharmacia Corporation, Corporate Patent Dept., 800 N. Lindbergh Boulevard - 04B, St. Louis, MO, 63167 Number of Claims: 48 CLMN Exemplary Claim: 1 ECL DRWN No Drawings LN.CNT 1452 CAS INDEXING IS AVAILABLE FOR THIS PATENT. US 2002071857 A1 20020613 DETD [0089] Such compositions are useful in treating inflammation in such diseases as migraine headaches, periarteritis nodosa, thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic fever, type I diabetes, neuromuscular junction disease including myasthenia gravis,. [0102] For pain management generally and specifically for treatment and DETD prevention of headache and migraine, such compositions of the invention can be used to provide a daily dosage of celecoxib of about 50 mg to. DETD [0110] In an embodiment of the invention, particularly where the cyclooxygenase-2 mediated condition is headache or migraine, the present selective cyclooxygenase-2 inhibitory drug composition is administered in combination therapy with a vasomodulator, preferably a xanthine derivative having. DETD . . . vasomodulator or alkylxanthine are selected to be therapeutically and/or prophylactically effective for relief of pain associated with the headache or migraine. Suitable dosage amounts will depend on the particular selective cyclooxygenase-2 inhibitory drug and the particular vasomodulator or alkylxanthine selected. For. IT 50-70-4, Sorbitol, biological studies 50-99-7, Glucose, biological 57-27-2, Morphine, biological studies 57-42-1, Meperidine studies 57-50-1, Sucrose, biological studies 63-42-3, Lactose 69-65-8, 69-79-4, Maltose 76-57-3, Codeine 87-99-0, Xylitol Mannitol 149-32-6, Erythritol 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, derivs. 9005-25-8, Starch, biological studies 9005-25-8D, Starch, derivs. 162011-90-7, Rofecoxib 169590-41-4, 181695-72-7, Valdecoxib 169590-42-5, Celecoxib **202409-33-4,** Etoricoxib 212126-32-4 215123-80-1 266320-83-6 (rapidly disintegrating oral formulation of cyclooxygenase-2 inhibitor)

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ANSWER 12 OF 14 USPATFULL on STN

2002:92708 USPATFULL

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ΤI
       Oral fast-melt dosage form of a cyclooxygenase-2 inhibitor
IN
       Kararli, Tugrul T., Skokie, IL, UNITED STATES
       Kontny, Mark J., Libertyville, IL, UNITED STATES
       Le, Trang T., Mundelein, IL, UNITED STATES
PΙ
       US 2000-226347P 20000819 (5)
Utility
       US 2002049233
                      A1 20020425
                                                                        <--
ΑT
PRAI
       Utility
DТ
       APPLICATION
FS
LREP
       Pharmacia Corporation, Corporate Patent Dept., 800 N. Lindbergh
       Boulevard - 04B, St. Louis, MO, 63167
CLMN
       Number of Claims: 39
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 1131
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       US 2002049233 A1 20020425
PΤ
DETD
       [0049] Such compositions are useful in treating inflammation in such
       diseases as migraine headaches, periarteritis nodosa,
       thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic
       fever, type I diabetes, neuromuscular junction disease including
       myasthenia gravis,. . .
DETD
       [0062] For pain management generally and specifically for treatment and
       prevention of headache and migraine, such compositions of the
       invention can be used to provide a daily dosage of celecoxib of about 50
DETD
       [0069] In an embodiment of the invention, particularly where the
       cyclooxygenase-2 mediated condition is headache or migraine,
       the present selective cyclooxygenase-2 inhibitory drug composition is
       administered in combination therapy with a vasomodulator, preferably a
       xanthine derivative having.
       . . . vasomodulator or alkylxanthine are selected to be
DETD
       therapeutically and/or prophylactically effective for relief of pain
       associated with the headache or migraine. Suitable dosage
       amounts will depend on the particular selective cyclooxygenase-2
       inhibitory drug and the particular vasomodulator or alkylxanthine
       selected. For.
IT
      50-70-4, Sorbitol, biological studies 57-27-2, Morphine, biological
      studies 57-42-1, Meperidine 57-50-1, Sucrose, biological studies
      57-55-6D, Propylene glycol, esters with fatty acids 63-42-3, Lactose
      69-65-8, Mannitol 69-79-4, Maltose 76-57-3, Codeine 87-99-0, Xylitol 151-21-3, Sodium lauryl sulfate, biological studies 577-11-7,
      Dioctyl sodium sulfosuccinate 585-88-6, Maltitol 7631-86-9, Silica, biological studies 25301-02-4, Tyloxapol 25322-68-3D, Polyethylene
      glycol, derivs. 106392-12-5, Poloxamer 162011-90-7, Rofecoxib
      169590-41-4, Deracoxib 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 202409-33-4, Etoricoxib 212126-32-4 215123-80-1 266320-83-6
        (oral fast-melt formulation of cyclooxygenase-2 inhibitor)
L7
     ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ΑN
     2001:780682 CAPLUS
DN
     135:335155
TI
     Rapid-onset formulation of a selective cyclooxygenase-2 inhibitors
ΙN
     Hariharan, Madhusudan; Kararli, Tugrul T.; Hassan, Fred; Forbes, James C.
PA
     Pharmacia Corporation, USA
SO
     PCT Int. Appl., 48 pp.
     CODEN: PIXXD2
DT
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LΑ
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                             APPLICATION NO.
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                         A1
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PRAI US 2000-197746P
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    WO 2001-US12434
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    MARPAT 135:335155
OS
RE.CNT
             THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
    WO 2001078724 A1 20011025
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                        KIND
                                           APPLICATION NO.
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                                           JP 2001-576024
     JP 2004500427
                         T2
                               20040108
                                                                   20010417
    An orally deliverable pharmaceutical composition is provided comprising a
AΒ
     selective cyclooxygenase-2 inhibitory drugs of low water solubility, for
     example celecoxib, and a glycol ether, for example diethylene glycol
    monoethyl ether. At least a substantial part of the drug is in dissolved
     or solubilized form in a solvent liquid comprising the glycol ether.
     composition has rapid-onset properties and is useful in treatment of
     cyclooxygenase-2 mediated conditions and disorders, particularly pain.
     For relief of pain in headache or migraine, the composition can
    optionally be administered together with a vasodilator. Solubility of
     celecoxib and valdecoxib in various solvent liqs. was studied. A soft
     gelatin capsule contained celecoxib 200, Labrasol 280, diethylene glycol
    monoethyl ether 280, and propylene glycol laureate 140 mg.
    58-08-2, Caffein, biological studies
                                          58-55-9, Theophylline, biological
IT
             69-89-6D, Xanthine, alkyl derivs. 83-67-0, Theobromine
     studies
     110-71-4, Ethylene glycol dimethyl ether 110-80-5, Ethylene glycol
    monoethyl ether
                     111-76-2, Ethylene glycol monobutyl ether 111-77-3,
    Diethylene glycol monomethyl ether 111-90-0, Diethylene glycol monoethyl
            111-96-6, Diethylene glycol dimethyl ether 112-36-7, Diethylene
    glycol diethyl ether
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    Triethylene glycol dimethyl ether 112-50-5, Triethylene glycol monoethyl
            112-73-2, Diethylene glycol dibutyl ether
                                                        122-99-6, Ethylene
    glycol monophenyl ether 124-07-2D, Caprylic acid, glycerides
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Triethylene glycol monobutyl ether 143-24-8, Tetraethylene glycol dimethyl ether 334-48-5D, Capric acid, glycerides 622-08-2, Ethylene glycol monobenzyl ether 629-14-1, Ethylene glycol diethyl ether 764-99-8, Diethylene glycol divinyl ether 18912-80-6, Diethylene glycol monoisobutyl ether 37321-62-3, Propylene glycol laurate 63980-40-5 68958-64-5, Polyoxyethylene glyceryl trioleate 156259-68-6, Capmul mcm 162011-90-7, Rofecoxib 169590-41-4, Deracoxib 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 202409-33-4, Etoricoxib 212126-32-4 215123-80-1 247074-38-0 266320-83-6 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (rapid-onset formulation of selective cyclooxygenase-2 inhibitors) ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN 2000:314539 CAPLUS 132:329940 Pharmaceutical compositions containing histaminergic agonist and COX-2 inhibitor for migraine treatment Simitchieva, Kremena; Reines, Scott A.; Mckinney, Errol; Sandquist, Eric J.; Khanna, Deepak K.; Hargreaves, Richard Merck & Co., Inc., USA PCT Int. Appl., 16 pp. CODEN: PIXXD2 Patent English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ______ ---------_____ -----Al 20000511 Wo 1999-US25388 19991029 <--WO 2000025779 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CA 2348979 AA20000511 CA 1999-2348979 19991029 <--EP 1126841 EP 1999-960171 20010829 A1 19991029 <---AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO JP 2002528498 20020903 Т2 JP 2000-579220 19991029 <--AU 759307 B2 20030410 AU 2000-17098 19991029 US 2002016348 Α1 20020207 US 2001-934823 20010822 <--

US 2001-934823 АЗ 20010822 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 9 ALL CITATIONS AVAILABLE IN THE RE FORMAT

20020507

20021128

19981102

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US 2002-106845

20020326 <--

В2

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TI Pharmaceutical compositions containing histaminergic agonist and COX-2 inhibitor for migraine treatment

PΙ WO 2000025779 Al 20000511

US 6384034

US 2002177617

US 1999-429274

WO 1999-US25388

PRAI US 1998-106605P

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PATENT NO. KIND DATE APPLICATION NO. DATE _____ ______ A1 20000511 WO 2000025779 PΙ WO 1999-US25388 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,

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                                            US 2002-106845
                          Α1
                                                                    20020326 <--
     A combination of a 5HT1B/1D agonist and a cyclooxygenase-2 (COX-2)
AΒ
     selective inhibitor is useful in the treatment and/or prevention of
     migraine. The 5HT1B/1D agonist is selected from sumatriptan,
     naratriptan, zolmitriptan, eletriptan, almotriptan, and rizatriptan, and
     the COX-2 inhibitor is selected from meloxicam, MK-663, Vioxx, RS 57067,
     celecoxib, and compound I. The 5HT1B/1D agonist and COX-2 inhibitor are
     administered combined in a single dosage form or as sep. dosage forms
     administered concurrently. Tablets containing 5 and 10 mg of rizatriptan
     benzoate and 10 mg Vioxx were prepared
ST
     cyclooxygenase inhibitor histaminergic agonist tablet migraine
IT
     5-HT agonists
        (5-HT1B; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
ΙT
     5-HT agonists
        (5-HT1D; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
IT
     Antimigraine agents
        (tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
IT
     Drug delivery systems
        (tablets; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
     39391-18-9, Cyclooxygenase
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (2, inhibitors; tablets containing histaminergic agonist and COX-2
        inhibitor for migraine treatment)
IT
     71125-38-7, Meloxicam 103628-46-2, Sumatriptan
                                                       121679-13-8,
     Naratriptan 139264-17-8, Zolmitriptan 143322-58-1, Eletriptan
     144034-80-0, Rizatriptan
                                145202-66-0, Rizatriptan benzoate
     154323-57-6, Almotriptan
                                162011-90-7, Vioxx
                                                     169590-42-5, Celecoxib
     179382-91-3, RS 57067
                            180200-69-5 202409-33-4, MK 663
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
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